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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SKIBINSKY, ANNA	

ART UNIT	PAPER NUMBER
1631	

MAIL DATE	DELIVERY MODE
03/03/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/621,821	KUTSYY ET AL.	
	Examiner	Art Unit	
	ANNA SKIBINSKY	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15,17,18 and 20-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15,17,18 and 20-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

REQUEST FOR CONTINUED EXAMINATION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/30/2007 has been entered.

Applicants' arguments, filed 10/30/2007 have been fully considered but they are not deemed persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Reply to Applicant's Amendments

Amendments to claim 15, 17 and 18 are acknowledged. Claims 1-14, 16 and 19 have been cancelled. Claims 15, 17, 18, 20- 26 are under examination.

Double Patenting

1. The provisional rejection of claims 15-26 for nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8 and 15-26 of copending

Application No.10/595,045 is withdrawn in view of Applicant's arguments filed 10/30/2007. Application No.10/595,045 was abandoned.

Claim Rejections - 35 USC § 103

1. This rejection is maintained from the previous Office Action filed 3/23/2007.

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. Claims 15, 17, 18, 20- 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Johnson (US Patent No. 6,611,833, filed June 23, 1999) in view of Friend et al. (US Patent No. 6,801,859, filed December 23, 1998).

4. As in instant claim 15, Johnson teaches a database of "blueprints" (i.e. captured images) of cellular tissue (i.e. population of cells) where statistical characteristics of tissue are collected after a population of tissue is profiled through imaging methods (col. 1, lines 45-56 and col. 2, lines 14-48). The tissues are profiled (i.e. signatures are created) and a plurality of structural indices are generated (col. 3, lines 5-59 and col. 4, lines 45-67) (i.e. metrics). The "group of cellular features" as recited in claim 15, would be any of the plurality of the cellular components within the sections of each tissue specimen from the subset taken during the imaging (col. 2, lines 25-32) and can include DNA or mRNA, cellular lipids or cellular ions (col. 4, lines 25-35). The distribution of measured characteristics (i.e. signatures) are calculated and stored for various types of

tissues such as “normal” and “abnormal” tissue (col. 5, lines 27-52). The “normal” and “abnormal” tissue as taught are from the same tissue population yet contain cellular features which are normal and abnormal, respectively, as required by claim 17. As recited in instant claim 15, the prior art of Johnson teaches the imaging (col. 2, lines 25-31 and col. 9. line 40 to col. 10, line 31) of a population of cells, creating signatures which are the measured characteristic for which an index, or metrics, are measured for “normal” tissue, and a side effect signature which is the characteristic (i.e. signature) of “abnormal” tissue that is either stored in the database or in the possession of the user (col. 21, lines 24-43). Johnson teaches making comparisons can be made between the features of the “normal” and “abnormal tissue”. The normal and abnormal tissue can then be accessed by a user who would like to compare samples to the tissues in the database.

5. As in instant claims 20-21, Johnson teaches deriving an “on-target metric” and “side effect metric” in the form of indices of “normal”, “abnormal”, and user introduced tissue. The metrics are the index values referred to throughout the text which are calculated from the various signature characteristics determined from the imaging. For example cellular DNA and mRNA characteristics and indexes are discussed (col. 15, lines 9-44). The control group (as recited in instant claim 20) is either the “normal” or “abnormal” tissue data in the database accessed by the user (col. 21, lines 24-43). The imaging (as recited in instant claim 21) is taught for profiling the tissue specimens (col. 3, lines 25-35).

6. Johnson teaches the measurement of qualitative data from cellular features determined from images. The data can be accessed by users to compare different states the tissue against the tissue in the database to determine it there has been a response which is "normal" or "abnormal", as in claim 20.

7. The prior art of Johnson teaches creating images of cells and then creating signatures and metrics for cells, as set forth above, but does not teach applying a treatment to the tissue (as recited in lines 1 and 3 of instant claim 15) and creating a signature that is an "on-target" signature and a "side effect signature" to characterize the treatment (as recited in lines 15 of instant claim 1). Though Johnson recites that the inventions can be used for drug development, he does not specifically recite varying the exposing the cellular tissue to treatment (instant claim 18). Johnson does not perform calculations in multivariate space (instant claims 22 and 23).

8. However, Friend et al. teaches obtaining a response profile for a compound such as a drug to determine if the compound exhibits an "ideal" vs. a "non-ideal" effect. The prior art of Friend et al. thus teaches treating cells with a drug to measure drug effectiveness and toxicity (col. 2, lines 42-62). The "ideal" effect is a measure of the "on-target effect" as required by claim 15 in that it relates to a consensus profile which represents an ideal, desired activity profile across some standard measurement set such as cellular constituents (i.e. cellular features from a cell population, as in claim 15), as required by claim 16. The "non-ideal" effect is a measure of the "side effect to the on target effect" in that Friend et al. teaches this to be a measure of related toxic effects of the treatment (col. 7, lines 1-14), as in claim 18. The calculation of a similarity "metric"

for comparing biological response profiles is also taught (col. 4, lines 27-38) by Friend et al. as required by claim 15.

9. Friend et al. further teach comparing the consensus profiles with the "ideal" drug effects and relative toxicity to evaluate the drug (col. 6, line 1-14), as in claim 15 requiring the comparison of the "on target effect" metric to the "side effect" metric to characterize the response of cells to the treatment.

10. Friend et al. teaches building "consensus profiles" for response of cells to various drugs by exposing them to graded levels of the drugs (col. 6, lines 1-19).

11. Friend et al. further teaches exposing cells to drug treatment, monitoring them for "ideal" and "non-ideal" effects, and based on generated profiles, identifies compounds with the desired activity (col. 6, lines 1-19 and col. 8, lines 19-51). Additionally, the calculation of metrics are specifically taught (col. 4, lines 27-38). The use of multivariate space is used to calculate the biological profiles (col. 12, lines 41-62). Data is clustered and the distances between the clusters is calculated (col. 20, lines 30-40).

12. Claims 24-26 recite characterizing the treatment is based on the side effect distance and the on-target effect distance and generating a graphical representation of the side effect distance and on-target effect distance.

13. Friend et al. teaches the calculation of distances of a cellular constituent affected by the treatment (col. 20, lines 30-40) which inherently characterizes the treatment. Graphical representations of data are taught in Figure 7.

14. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have implemented the teachings of Johnson where

images of “normal” and “abnormal” cell tissues are taken and the characteristics of (signatures) of cellular features are measured to form indices (metrics) that can be accessed and used for comparison, in combination with the teachings of Friend where effectiveness (on site effect signature) and toxicity (side effect signature) are measured. One of skill in the art would have been motivated to modify the teachings of Johnson with that of Friend because Friend teaches that such methods are useful in the process of drug discovery or design (col. 2, line 63 to col. 3, line 9). One of skill in the art would have had a reasonable expectation of success at using the imaging and measurement of quantitative characteristics of cells as taught by Johnson et al. (col. 1, lines 45-56 and col. 2, lines 14-48) on the drug candidate treated cells of Friend et al. because both Johnson and Friend treat analysis of cellular constituent characteristics.

REPLY TO REMARKS

15. Applicant's arguments filed 10/30/2007 have been fully considered but they are not persuasive.

16. Applicants argue (Remarks, page 9, lines 9-11) that Johnson does not teach characterizing first and second groups of cellular features elected from a single plurality of cellular features derived from a population of cells, as claimed.

17. In response, it is noted that claim 15 recites creating an on target effect signature from a group of cellular features and creating a side effect signature from a second group of cellular features (claim 15, lines 6-10). Johnson teaches that tissues are profiled (i.e. signatures are created) and a plurality of structural indices are generated

(col. 3, lines 5-59 and col. 4, lines 45-67) (i.e. metrics). The distribution of measured characteristics (i.e. signatures) are calculated and stored for various types of tissues such as "normal" and "abnormal" tissue (col. 5, lines 27-52). The "group of cellular features" as recited in claim 15, would be any of the plurality of the cellular components within the sections of each tissue specimen from the subset taken during the imaging (col. 2, lines 25-32) and can include DNA or mRNA, cellular lipids or cellular ions (col. 4, lines 25-35). As such, the cellular features of normal and abnormal tissue (i.e. first and second group of cellular features) are characterized when the profiles are created, as argued by applicants.

18. Applicants argue (Remarks, page 9, lines 12-15) that Johnson does not teach "comparing the on-target effect metric to the side effect metric" in which both of those metric are obtained from first and second groups of cellular features selected form a single plurality of cellular features derived from a population of cells.

19. In response, Johnson teaches obtaining a metric wherein a plurality of structural indices are generated (col. 3, lines 5-59 and col. 4, lines 45-67) (i.e. metrics) for a population of cells that contain normal and abnormal tissue. Johnson et al. does not however teach an "on target effect" and "side effect" from which the metric would be derived. However, Friend et al. teaches obtaining a response profile for a compound such as a drug to determine if the compound exhibits an "ideal" vs. a "non-ideal" effect on cells. Friend et al. teachings of (col. 2, lines 42-62) the "ideal" effect reads on the measure of the "on-target effect" as required by claim 15 in that it relates to a consensus profile which represents an ideal, desired activity profile across some

standard measurement set such as cellular constituents (i.e. cellular features from a cell population, as in claim 15). The "non-ideal" effect reads on the a measure of the "side effect" in that Friend et al. teaches this to be a measure of related toxic effects of the treatment (col. 7, lines 1-14), as in claim 18. The calculation of a similarity "metric" for comparing biological response profiles is also taught (col. 4, lines 27-38) by Friend et al. as required by claim 15.

20. Applicants argue (Remarks, page 9, line 17 to page 10, line 13) that Friend et al. do not teach an "on-target effect signature" of a treatment on the population of cells or a "side effect signature" of a treatment on the population of cells. Applicants further argue that Friend does not teach characterizing first and second groups of cellular features selected from a single plurality of cellular features derived from a population of cells as claimed.

21. In response, the creation of signatures for cellular features is taught by Johnson. Johnson however does not teach signatures for cells treated with a drug and wherein cellular features experience an "on target effect" and a "side effect" of the drug. Friend et al. however teach measuring the "ideal" effect (col. 2, lines 42-62) which reads on the measure of the "on-target effect" on cellular features that the "ideal" effect relates to a consensus profile which represents an ideal, desired activity profile for cellular constituents (i.e. cellular features from a cell population, as in claim 15). The "non-ideal" effect as taught by Friend et al. reads on the a measure of the "side effect" in that Friend et al. teaches this to be a measure of related toxic effects of the treatment (col. 7, lines 1-14). Furthermore, the claim 15 recites "a population of cells" but does not limit this

population to being a certain type. Johnson et al. teaches creating signatures and metrics for normal and abnormal cells that come from the same type of tissue. Thus the teaching of Johnson et al. reads on creating signatures for "a population of cells". As in any population, there may be sick or healthy, or a plurality of different individuals. Therefore the “population of cells” is broadly interpreted as being any number of cells that are being measured in the method of Johnson or Friend et al.

22. Applicants argue that nothing in Johnson or Friend suggest modifying or combining the teachings of the references to arrive at the claimed invention.

23. In response, it would have been obvious to one of skill in the art of create “signatures” in the form of profiles and from these a “metric” in the form of structural indices as taught by Johnson (col. 3, lines 5-59 and col. 4, lines 45-67) for a group of cells (i.e. a population) that has been treated with a drug and exhibiting "idea" (i.e. on-target) and "on-ideal" (side effect) responses to the treatment. One of skill in the art would have been motivated to modify the teachings of Johnson with that of Friend because Friend et al teach that their method is useful in the process of drug discovery or design (col. 2, line 63 to col. 3, line 9), as set forth above.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anna Skibinsky whose telephone number is (571) 272-4373. The examiner can normally be reached on 8 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjie Moran can be reached on (571) 272-7020. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

2/28/08

Anna Skibinsky, PhD

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